NGR-50-002-083
Univ. of Wisconsin

# A Model of Renal Function

J. Gianunzio

Any model of the cardiovascular system concerned with the flow of substances carried by the blood should contain a model of kidney function. The kidney plays a very important role in regulating the composition and volume of the internal fluid environment. A good review of renal structure and function can be found in Pitts (3), Selkurt (4), and Smith (5). In this paper a model of the kidney based on the major hypotheses of renal function is described.

The hypotheses and assumptions from which a kidney model is formulated are listed below.

1) Glomerular filtration is an ultrafiltration which depends on the hydrostatic pressure of the blood. The rate of glomerular filtration $\dot{Q}_f$ is related to the pressure drop across the capillary membrane $\Delta p$ by the following.

$$\dot{Q}_f = K_f \, \Delta p$$

where $K_f$ is a constant expressing fluid permeability of the glomerular capillary membrane.

2) The loops of Henle act as countercurrent multipliers in the formation of concentrated urine.

3) The medullary blood vessels remove water and solutes from the countercurrent area.

4) The countercurrent mechanism depends on the active transport of sodium and other solutes. Water moves in the system by passive diffusion.

5) Since renal capillaries and tubules have very small diameters, inertial effects on fluids flowing in them may be neglected.

6) There is complete mixing of substances in the blood and urine.

The kidney contains approximately one million nephrons. In the model the effects of all nephrons acting in parallel are lumped to form a single average effect. In this initial model there is no distinction made between cortical and juxtamedullary nephrons. If necessary, this feature could be added without much difficulty. The average nephron as shown in Figure 1 is the basis for the model.

A discussion of the principle of countercurrent multiplication can be found in the references given previously. It is also treated quite thoroughly in a paper by Ullrich, Kramer and Boylan (6). As shown in Figure 1, $Na^+$ is actively transported out of the ascending limb of the loop of Henle into the interstitial fluid and then into the descending limb by passive diffusion. The thick part of the ascending loop is impermeable to water. This process multiplied along the length of the tubule results in a hypertonic solution at the tip of the loop of Henle. Water is then drawn from the collecting duct into the interstitium in the zone of hyperosmolality established by the countercurrent multiplier system. This results in a more highly concentrated urine. Sodium and other solutes taken out of the tubule are removed by the vasa recta system of blood vessels. Water is also absorbed by the vasa recta due to the colloid osmotic pressure of plasma protein.

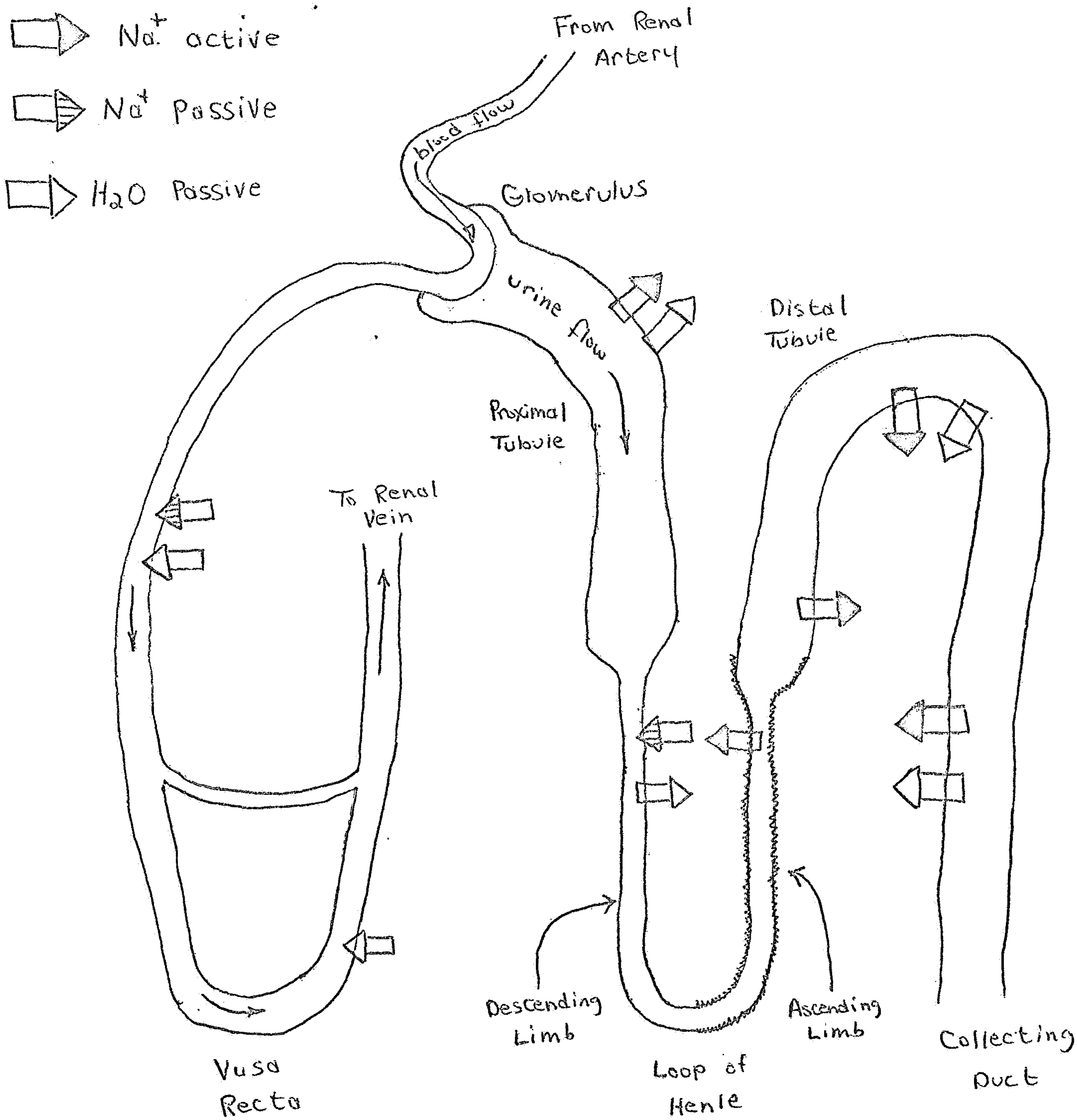


Fig 1 - The Nephron and Vasa Recta

An electrical circuit analog for the pressure-flow relations in the kidney model is shown in Figure 2. The lumped parameter approximation of a cylindrical vessel as developed by Rideout and Dick (2) is used to represent the blood vessels and tubules. The equations relating pressure p, flow f, and volume q for a typical section of the model are listed below.

$$q_{11tot} = \int_o^t (f_{11} - f_{12} - f_{15})dt + q_{11tot}(0)$$

$$p_{11} = \frac{1}{C_{11}}(q_{11tot} - q_{11u}) = \frac{q_{11}}{C_{11}}$$

$$f_{11} = \frac{1}{L_{11}}\int_o^t (p_6 - p_{11} - R_{11}f_{11})dt$$

The electrical parameters resistance R, capacitance C, and inductance L represent resistance to flow, compliance of the vessel and inertance of the fluid. Osmotic pressure is approximated by the voltage source ( $^{+}E^{-}$ ).

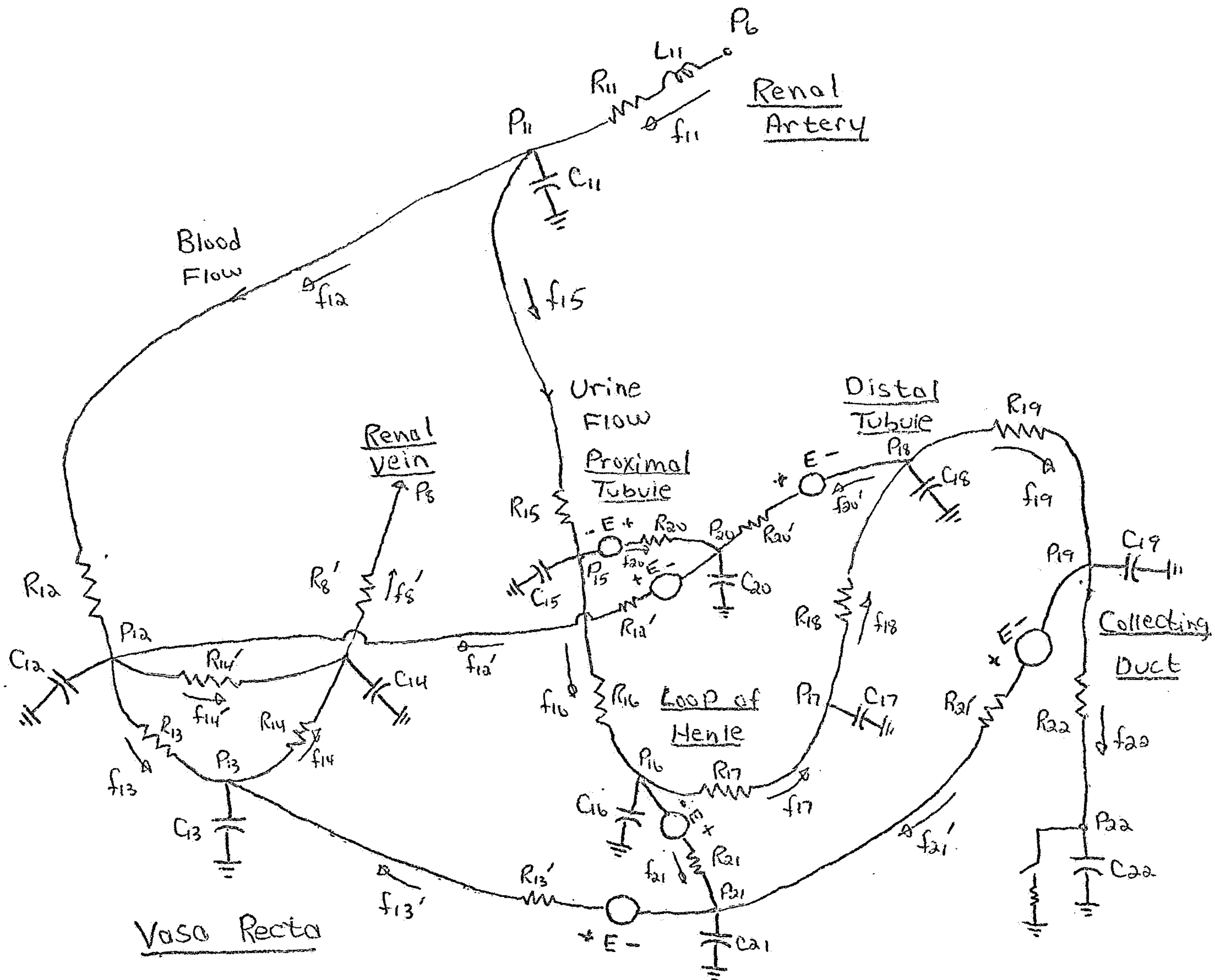


Fig 2 - An Electrical Circuit Representation of the Pressure-Flow Relations in the Nephron and Renal Blood Vessels.

## Glossary of Terms

| | |
|---|---|
| $L_{11}$ | Inertance in renal artery |
| $R_{11}$ | Resistance to flow in renal artery |
| $R_{15}$ | Resistance to flow across glomerular capillary membrane ($= 1/K_f$) |
| $R_{16}$, $R_{17}$, $R_{18}$, $R_{19}$, $R_{22}$ | Resistances in the nephron |
| $R_{12}$, $R_{13}$, $R_{14}$, $R_{14}'$, $R_8'$ | Resistances in the renal blood vessels |
| $R_{20}$, $R_{20}'$, $R_{12}'$, $R_{21}$, $R_{21}'$, $R_{13}'$ | Resistances to movement of water from nephron and capillaries to the interstitium |
| $C_{11}$ | Compliance of renal artery |
| $C_{15}$ | Compliance of proximal tubule |
| $C_{16}$ | Compliance of descending limb of Henle's loop |
| $C_{17}$ | Compliance of ascending limb of Henle's loop |
| $C_{18}$ | Compliance of distal tubule of Henle's loop |
| $C_{19}$ | Compliance of collecting duct |
| $C_{20}$ | Compliance of bladder |
| $C_{20}$,$C_{21}$ | Compliances of interstitial fluid compartments |
| $C_{12}$, $C_{13}$, $C_{14}$ | Compliances of medullary blood vessels |

An electrical analog circuit for the complete cardiovascular system is shown in Figure 3. As stated previously this model relates pressures, flows and volumes but gives no information as to the concentrations of substances in the blood and urine. A possible method of simulating the distribution of a specific substance in the blood and urine is the "multiple model" scheme of Beneken and Rideout (1) in which separate but interconnected circuits are used for the blood-urine pressure-flow relations and the transport of the substance of interest. The latter circuit consists of a number of compartments equal to the number of segments in the blood-urine circuit. Since complete mixing is assumed, the concentration of a substance in the blood or urine is uniform in a particular compartment.

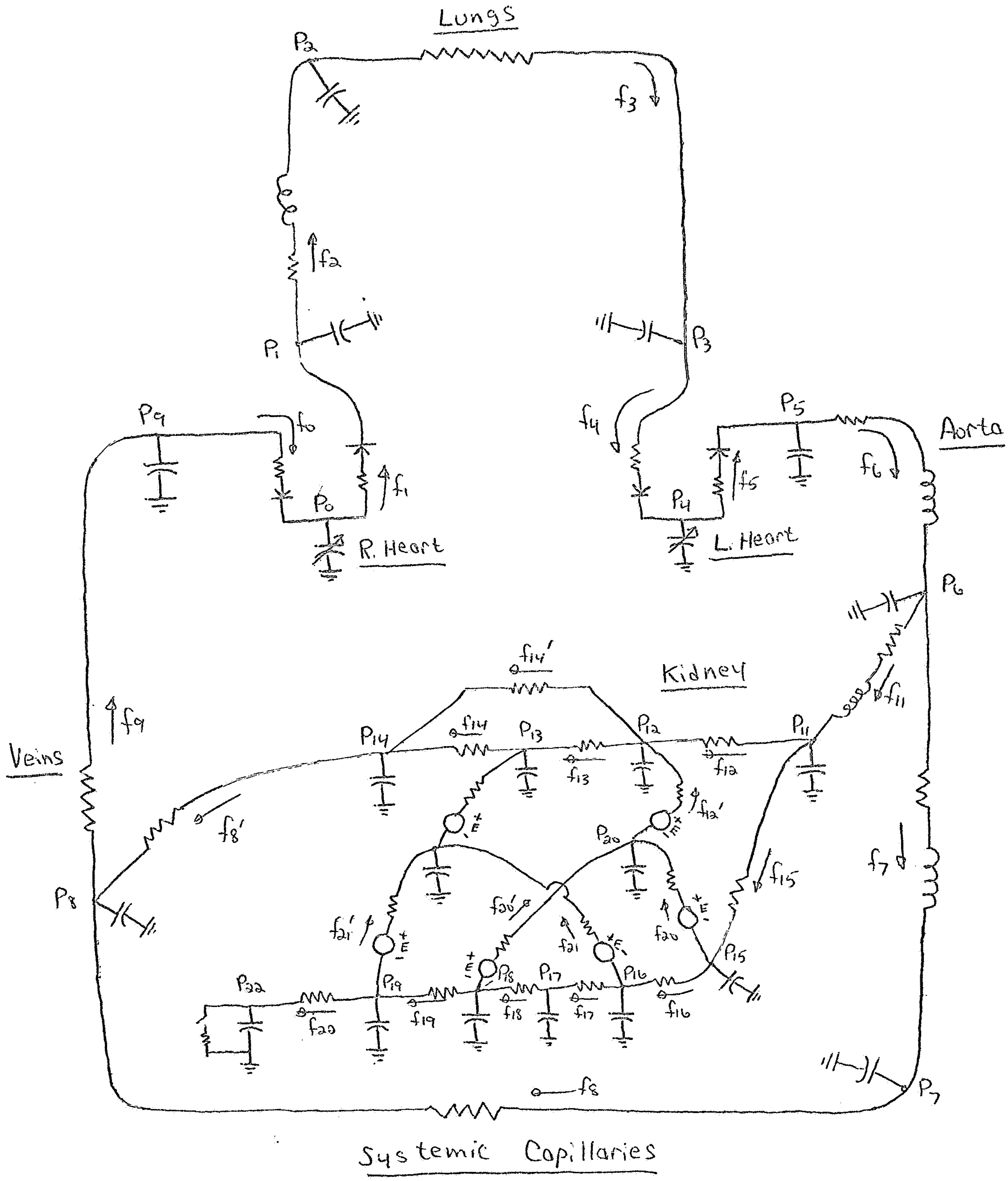


Fig 3 – An Electrical Circuit For the Pressure-Flow Relations in the Complete Cardiovascular Loop.

The equations for the flow of a substance between two compartments are listed below.

$$\alpha_2 = \int_0^t (\gamma_{1,2}f_2 - \gamma_{2,3}f_3)dt + \alpha_2(0)$$

$$\gamma_{1,2} = \gamma_1 \quad \text{if} \quad f_2 > 0$$

$$= \gamma_2 \quad \text{if} \quad f_3 < 0$$

$$\gamma_{2,3} = \gamma_2 \quad \text{if} \quad f_3 > 0$$

$$= \gamma_3 \quad \text{if} \quad f_3 < 0$$

$$\gamma_2 = \alpha_2/q_{2tot}$$

$$q_{2tot} = \int_0^t (f_2 - f_3)dt + q_{2tot}(0)$$

where $\gamma_n$ is the concentration of the substance in compartment n, $\alpha_n$ is the amount of the substance in n and $q_n$ is the volume of blood in in compartment n, $f_n$ is the flow into n and $f_{n+1}$ is the flow out of n. At the points where branching occurs, slight modification of the multiple model equations are necessary. For example, consider the point where the renal artery branches off.

$$\alpha_6 = \int_o^t (\gamma_5 f_6 - \gamma_6 f_7 - \gamma_6 f_{11})dt + \alpha_6(0)$$

$$q_{6tot} = \int_o^t (f_6 - f_7 - f_{11})dt + q_{6tot}(0)$$

$$\gamma_6 = \frac{\alpha_6}{q_{6tot}}$$

Active and passive transport of substances in the kidney require that additional terms be added to the multiple model equations. The passive diffusion of a substance between two compartments is given by:

$$\frac{d\alpha_n}{dt} = - K_n(\gamma_n - \gamma_{n+1}) \qquad \text{(Fink's Equation)}$$

where $K_n$ is a diffusion constant. The active transport of sodium out of a compartment is given by:

$$\frac{d\alpha_n}{dt} = - A_{Na}$$

where $A_{Na}$ is the rate of active transport of sodium and is dependent on the concentration of sodium in compartment n, the concentration in the compartment into which it is transported and the length of time the fluid containing sodium remains in compartment n.

As an example consider compartment 15.

$$\alpha_{15} = \int_o^t (\gamma_{11}f_{15} - \gamma_{15}f_{16} - A_{Na20})dt + \alpha_{15}(0)$$

$$q_{15tot} = \int_o^t (f_{15} - f_{16} - f_{20})dt + q_{15tot}(0)$$

$$\gamma_{15} = \alpha_{15}/q_{15tot}$$

As an example of passive diffusion of sodium consider compartment 12.

$$\alpha_{12} = \int_o^t (\gamma_{11}f_{12} - \gamma_{12}f_{14}' - \gamma_{12}f_{13} - K_{Na}\gamma_{20})dt + \alpha_{12}(0)$$

$$q_{12tot} = \int_o^t (f_{12} + f_{12}' - f_{13} - f_{14}')dt + q_{12tot}(0)$$

$$\gamma_{12} = \frac{\alpha_{12}}{q_{12tot}}$$

Figure 4 shows a compartment model for the transport of sodium in the kidney. The rates and directions of sodium flow are indicated. The dashed line represents the active transport of sodium from the ascending loop of Henle which is impermeable to water. Each substance studied requires a separate transport circuit. Thus, if the simulation is set up on the hybrid computer, the number of substances which can be studied simultaneously is limited by available computer equipment.

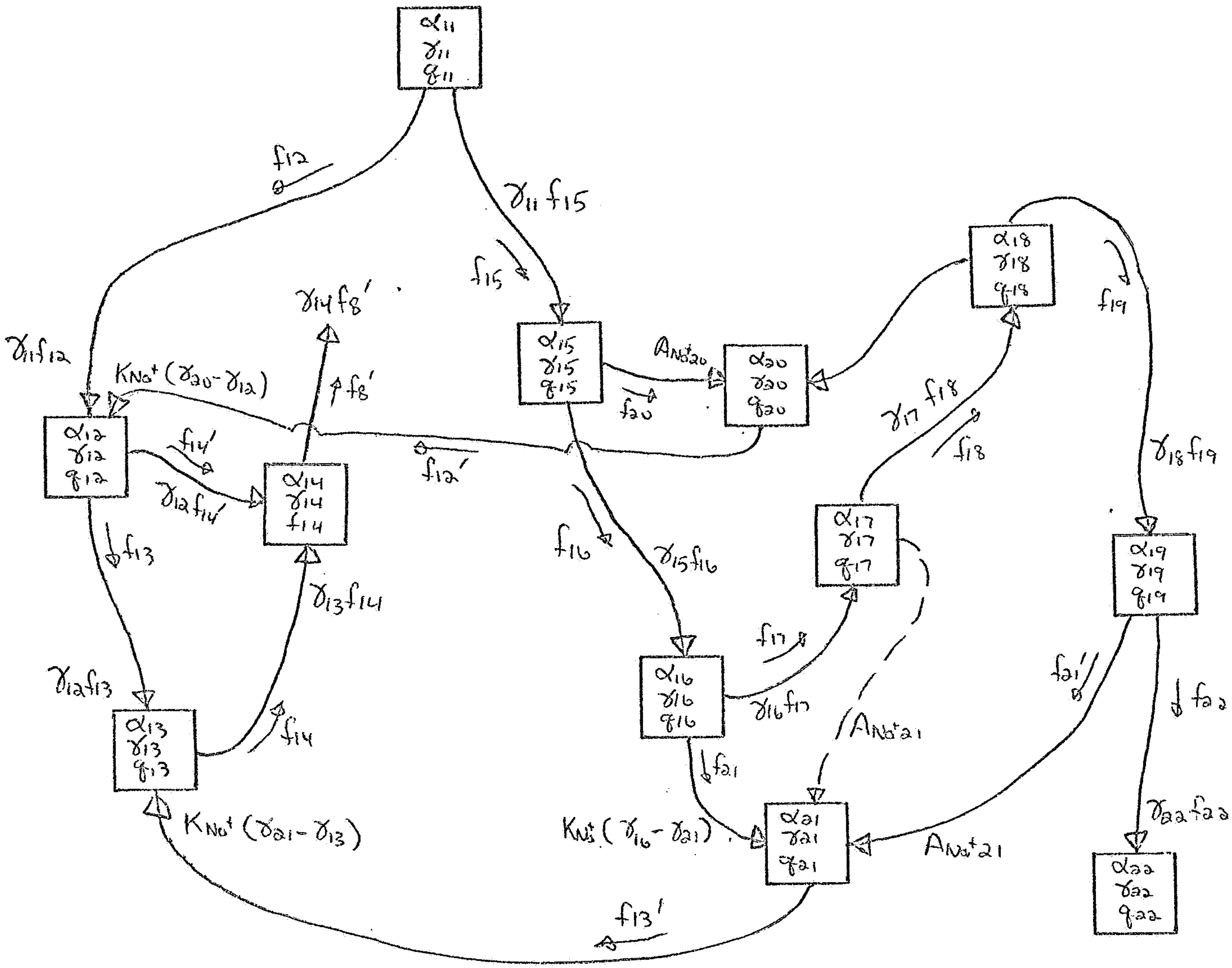

Fig 4 - A Compartment Model
For $Na^+$

## References

1. Beneken, J. E. W. and V. C. Rideout, "The Use of Multiple Models in Cardiovascular System Studies: Transport and Perturbation Methods," University of Wisconsin, Department of Electrical Engineering, Madison.

2. Dick, D. E. and V. C. Rideout, "Analog Simulation of Left Heart and Arterial Dynamics," Presented at the 18th Annual Conference on Engineering in Medicine and Biology, Philadelphia, November, 1965.

3. Pitts, R. F., Physiology of the Kidney and Body Fluids, Year Book Medical Publishers, Chicago, 1963.

4. Selkurt, E. E., "Renal Function," Physiology, E. E. Selkurt ed., Little, Brown and Company, Boston, 1966, 489-520.

5. Smith, H. W., Principles of Renal Physiology, Oxford University Press, New York, 1956.

6. Ullrich, K. J., K. Kramer and J. W. Boylan, "Present Knowledge of the Counter-Current System in the Mammalian Kidney," Heart, Kidneys and Electrolytes, C. K. Friedberg ed., Greene and Stratton, 1962.